

REMARKS

The undersigned thanks Examiner Lu for the courtesies extended during the interview of July 26, 2007. During the interview, the Examiner provided a few very helpful suggestions. For example, the Examiner suggested reciting “aligning the coded probes that bind to the one or more target molecules on a surface by microfluidic molecular combing” in claims 1 and 19. This limitation is supported the limitation of original claims 9 and 20. In addition, the Examiner suggested providing the attached article entitled “Molecular Combing” to clarify that the term “molecular combing” is known in the art to mean “to stretch macromolecules (among which DNA) in a parallel fashion, by anchoring them specifically by their extremities.” This meaning of “molecular combing” is consistent with “molecular combing” shown in Figures 10 and 11, which show coded probes that have been straightened by microfluidic flow. On the other hand, Figure 9 shows coded probes arranged randomly without having been straightened by microfluidic flow. New claims 29-32 are supported by paragraph [0096] which discloses “electrophoresis” as an additional method for aligning the coded probes.

During the interview, the undersigned presented the arguments made below to overcome the obviousness rejection. The Examiner stated that the obviousness rejection will be withdrawn in light of these arguments.

Claim Rejection - 35 U.S.C. §112

Claims 11 and 24 were rejected under 35 USC 112, second paragraph. This rejection is respectfully traversed and should be withdrawn in light of the pending Amendment as “process” has been changed to “equipment” in claim 11 and “before” has been changed to “after” in claim 24.

Claim Rejection - 35 U.S.C. §103

Claims 1-6, 9 and 15-18 were rejected as being obvious over Mirkin. This rejection is respectfully traversed.

The Examiner cites Example 6 in column 85 and 86, and Figure 13B, of Mirkin to argue that Mirkin discloses the embodiments of the inventions of claims 1 and 19. See page 5, lines 1-19, of the Action of April 16, 2007. Claims 1 and 19, as amended, recite “aligning the coded probes that bind to the one or more target molecules on a surface by microfluidic molecular combing.” Mirkin fails to teach or disclose this limitation. Applicants respectfully explain why.

In Mirkin, SEQ ID. NO: 33 and SEQ ID. NO: 34 are very short molecules having 12 base pairs and 24 base pairs, respectively, attached to gold nanoparticles of 13 nm diameter. [See Example 6 of Mirkin, column 86, lines 19-24, and line 29.] As the spacing between two adjacent base pairs is 0.34 nm, the lengths of SEQ ID. NO: 33 and SEQ ID. NO: 34 are:

$$\text{SEQ ID. NO: 33} = 12 \times 0.34 \text{ nm} = 4.08 \text{ nm}$$

$$\text{SEQ ID. NO: 34} = 24 \times 0.34 \text{ nm} = 8.16 \text{ nm}$$

On the other hand, the diameter of Mirkin's gold nanoparticles is 13 nm. As a result, as shown in Figure 13B of Mirkin, the DNA strands with SEQ ID. 33 and SEQ ID. 34 of lengths 4.08 nm and 8.16 nm, respectively, stick out from the spherical gold nanoparticles of 13 nm diameter like short hairs on a ball. The substrate of Mirkin is the flat “transparent substrate” shown in Figure 13B. Persons of ordinary skill in this art would immediately recognize that it is *impossible* in Mirkin for the DNA strands of lengths 4.08 nm and 8.16 nm that stick out from the spherical gold nanoparticles of 13 nm diameter to be aligned so as to straighten the coded probes on the flat transparent substrate surface shown in Figure 13B of Mirkin by application of microfluidic flow. In Mirkin, there is *no* application of microfluidic flow. In addition, there is no alignment of coded probes so as to straighten the coded probes by application of microfluidic flow. Thus, Mirkin does not teach or suggest “aligning the coded probes that bind to the one or more target molecules on a surface by microfluidic molecular combing” as recited in claims 1 and 19.

Mirkin also does not teach or suggest “two or more identifiably different nano-barcodes that create different signatures” as recited in claims 1 and 19. Instead, Mirkin teaches different

probe molecules connected to nanoparticles that function *only* as amplifiers of the signal. In the embodiments of the present invention, the two or more identifiably different nano-barcodes that create different signatures could function as *both* amplifiers and identifiers.

Claims 7 and 8 were rejected as being obvious over Mirkin in view of Birkenmeyer. This rejection is respectfully traversed.

Birkenmeyer does not fill the gaps in Mirkin that are stated above. Also, claims 7 and 8 depend indirectly from claim 1. As claim 1 should now be allowable, so claims 7 and 8 should also now be allowable.

Claims 10-14 were rejected as being obvious over Mirkin in view of Nygren. This rejection is respectfully traversed.

Nygren does not fill the gaps in Mirkin that are stated above. Claims 10-14 depend indirectly from claim 1. As claim 1 should now be allowable, so claims 10-14 should also now be allowable.

Claims 19-23 were rejected as being obvious over Mirkin in view of Nygren. This rejection is respectfully traversed.

As explained above, Mirkin does not teach or suggest “aligning the coded probes that bind to the one or more target molecules on a surface by microfluidic molecular combing” as recited in claim 19. Mirkin also does not teach or suggest “two or more identifiably different nano-barcodes that create different signatures” as recited in claim 19. Nygren fails to fill these gaps in Mirkin.

